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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/931,701	08/16/2001	Helle Outtrup	10065.200-US	3473

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EXAMINER	
MOORE, WILLIAM W	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/931,701	OUTTRUP ET AL.	
	Examiner	Art Unit	
	William W. Moore	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-11,14,19-23,29-41,48 and 49* is/are pending in the application.

4a) Of the above claim(s) *23,29-41 and 48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-8,14,19-22 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,2,6-11,14,19-23,29-41,48 and 49* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 60/235,459.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/7/02 & 2/7/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statements

Information Disclosure Statements were filed in this application on July 1, 2002, and on July 2, 2004. The former provided a single page of PTO Form-1449 citing two US Patents and three published PCT applications. The latter provided two pages of PTO Form-1449 wherein the first page cites the five publications cited in the first Information Disclosure Statement and the second page cites no publications. To avoid redundancy of citation on the face of any patent that may issue on this application, only an executed copy of the PTO Form-1449 that accompanied the Information Disclosure Statement filed July 1, 2002, is supplied and made of record in this communication.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. §121:

1. Claims 1, 2, 6-11, 14, 19-22 and 49, drawn to a subtilase serine protease, to compositions comprising same, and to a method of producing same by culturing a strain of *Bacillus* to produce a supernatant comprising the protease and isolating the protease from the supernatant, classified, *inter alia*, in class 435, subclass 221.
2. Claims 23, 29-41, and 48, drawn to a polynucleotide comprising a nucleic acid sequence encoding a subtilase serine protease, to vectors that comprise the polynucleotide, to host cells transformed with the polynucleotide, and to a method of making the encoded protease by culturing a transformed host cell under conditions suitable for the expression thereof, classified, *inter alia*, in class 536, subclass 23.2.

Inventions of Groups 1 and 2 are related as product and process of making. The inventions can be shown to be distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product as claimed can be made by another and materially different process such as solid phase chemical synthesis.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification restriction for examination purposes as indicated is proper.

During a telephone conversation with Mr. Elias J. Lambiris on November 32, 2004, a provisional election was made with traverse to prosecute the invention of Group 1, claims 1, 2, 6-11, 14, 19-22 and 49. Affirmation of this election must be made by applicant in replying to this Office action. Claims 23, 29-41, and 48 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR §1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR §1.48(b) and by the fee required under 37 CFR §1.17(h).

Notice of Requirements for Rejoinder

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier.** Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. §§101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order

to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. §121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim Rejections - 35 USC § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 2, 6 and 7 are rejected under 35 U.S.C. § 101 because the claimed invention is not directed to statutory subject matter.

A claimed invention may not be described as a product of Nature as it exists in Nature but must instead distinguish a new and useful composition of matter from a product of Nature by a description disclosing that a composition is isolated from Nature. Amending claim 1 to recite "an isolated subtilase", or "a substantially pure subtilase", will overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 8-11, 14, 19-22 and 49 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to exemplify or describe the preparation of subject matters that are generic, non-functional, proteins of claims 1, 2, 8-11 and 14, compositions of

claims 19-22 that comprise such generic proteins, or proteins produced by the method of claim 49. According to the preamble and clauses of the claim 1, a "subtilase" need only be a protein having some degree of structural relationship to SEQ ID NO:2, to an amino acid sequence encoded by a nucleic acid sequence hybridizable "under low stringency conditions" with an 807 nucleotide sequence of SEQ ID NO:1, or to a lesser portion of at least 100 nucleotides thereof. But neither the preamble nor clauses of the claim require divergent proteins to have the serine protease activity provided by the amino acid sequence of SEQ ID NO:2 and the specification does not disclose the multitude of amino acid sequence alterations that differentiate between the myriad of divergent proteins that function as serine proteases and the myriad proteins that do not.

Further, according to clause (b) of the claim, serine proteases "encoded by a nucleic acid sequence [hybridizing] under low stringency conditions with [either] a complementary strand of the nucleic acid sequence of nucleotides [from position] 334 to [position] 1140 of SEQ ID NO:1, or a subsequence of [the 807 nucleotide sequence] of at least 100 nucleotides" are included. Yet the clause defines no "low stringency" conditions and such conditions may permit, *arguendo*, the hybridizing, generic protease-encoding, sequences to share as little as 70% identity at the nucleic acid sequence level where sequence non-identity need not be distributed evenly throughout codons. Thus claims 1, 2, 8-11 and 14 include proteases encoded by nucleic acid sequences where non-identity occurs at first codon positions and the resulting protease amino acid sequences may diverge as much as 90% from identity with the amino acid sequence of SEQ ID NO:2, i.e., sharing just 10% identity with SEQ ID NO:2.[1] Clause (b)(ii) of claim

[1] Calculated by taking the 807 nucleotides of SEQ ID NO:1 that encode the 269 amino acid sequence of SEQ ID NO:2 X 30% nonidentity [807x 0.3] = 242 altered nucleotides. Where no claim places a structural limitation on locations of altered nucleotides and alterations occur at first codon positions, the 242 altered codons may specify 242 relative amino acid substitutions and the resulting protease amino acid sequence need share only (269-242)/269 = 0.100 = 10% identity with the amino acid sequence of SEQ ID NO:2.

1 describes a near absence of structural limitation because it permits a polynucleotide encoding only 33 of the 269 amino acids of SEQ ID NO:2 to be the basis for defining amino acid sequences of other proteases where the complement of any sequence of 100 nucleotides within the boundaries of clause (b)(i) hybridizes under conditions of low stringency with a protease-encoding polynucleotide. Such a hybridizing nucleic acid sequence may encode a protease sharing just 3 out of the 269 amino acids of SEQ ID NO:2 - 1.1% amino acid sequence identity with SEQ ID NO:1 - where resulting protease amino acid sequences diverge at as many as 30 amino acid sequence positions within an unspecified, internal, array of 33 contiguous amino acids of SEQ ID NO:2 that were encoded by the selected 100-nucleotide region while diverging completely elsewhere. While claim 8 does not depend from claim 1, it is also rejected because it states no structural limitation defining the extent of structural alteration of the amino acid sequence of SEQ ID NO:2.

Neither the claims nor the specification disclose or teach where so many amino acid sequence alterations might occur nor what they might be, and the specification does not otherwise disclose or suggest the nature or source of the myriad generic proteases that meet the limitations of the claims. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. § 112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601 at 1605 (Fed. Cir. 1993). Nothing demonstrates that, at the time the specification was filed, Applicant was "able to envision" enough of the structure of the undisclosed generic proteases of the elected claims to provide the public with identifying "characteristics [that] sufficiently distinguish [them] from other materials". *Fiers*, 25 USPQ2d at 1604 (citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). The treatment

of the claimed subject matter in the specification is considered to be entirely prospective where skilled artisans in the relevant field of molecular biology could not predict the structures, or other properties, of proteases of claims 1, 8, and 14, proteases in compositions of claims 19-22, or proteases produced by a method of claim 49.

Claims 1, 8-11, 14, 19-22 and 49 are rejected under 35 U.S.C. § 112, first paragraph, because the specification is not enabling for the design and preparation of a protease having an amino acid sequence diverging from the sequence set forth in SEQ ID NO:2 by amino acid substitutions, deletions and insertions, or combinations thereof at as many as 90% of the amino acid positions therein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, make and use the invention commensurate in scope with these claims.

Claims 1, 8-11, 14, 19-22, and 49 contemplate arbitrary assignments of any or all of amino acid substitutions, additions or deletions in a protease comprised by a claimed composition at as many as 90% of the amino acid positions in its primary structure. Yet, as explained above, the specification fails to support introduction of as many as 242 amino acid sequence alterations in the sequence of SEQ ID NO:2 permitted by claims 1,14, 19-22, and 49 where insertions, deletions, or substitutions occur anywhere, in any combination or pattern, in SEQ ID NO:2. Indeed, neither the specification nor the prior art made of record, taken together, can identify 242 amino acids in subtilase amino acid sequences that might be altered, nor teach the nature of an alteration that may be made, which permits a resulting polypeptide to function as a protease. While claims 8-11 do not depend from claim 1, they are rejected because they state no limitation to the extent of structural alteration of the amino acid sequence of SEQ ID NO:2. Mere sequence perturbation cannot enable design and preparation of nucleotide sequences encoding a myriad of divergent protease enzymes and provide the public with a nucleotide sequence encoding an enzyme that retains its native function.

It is well settled that 35 U.S.C. § 112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed

without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (recognizing and applying the "*Forman*" factors). Cf., *Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986) (citing eight factors relevant to analysis of enablement). The standard set by the CCPA, the precursor of the Court of Appeals for the Federal Circuit, is not to "make and screen" any and all possible alterations because a reasonable correlation must exist between the scope asserted in the claimed subject matter and the scope of guidance the specification provides. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with the degree of unpredictability of factors involved in physiological activity of small peptide hormone). The Federal Circuit approved the standard set by the CCPA in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997). Applying the factors of the analysis the court applied in *Wands*, ***supra***, to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering the amino acid sequence of the protease of SEQ ID NO:2 to the extent permitted by clause (b) of claim 1,

b) the specification lacks working examples where the amino acid sequence of SEQ ID NO:2 is altered to the extent recited in the claims,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such alteration, and,

d) unpredictability exists in the art where no members of the class subtilase proteases represented by the amino acid sequences of SEQ ID NO:2 have had as many as 242 amino acids specifically identified for concurrent modification.

The scope of proteases embraced by clause (b) of claim 1 "encoded by a nucleic acid sequence which hybridizes under low stringency conditions with . . . a complementary strand of the nucleic acid sequence of nucleotides 334 to 1140 of SEQ ID NO:1, or, a subsequence of at least 100 nucleotides", is unsupported by the present specification even if taken in combination with teachings available in the prior art.

Claim 49 presents a separate issue of enablement because it describes a culture of untransformed *Bacillus* cells that can secrete a disclosed subtilase and the specification discloses such a culture to be a specific biological material, the *Bacillus clausii* strain DSM 13585. The specification does not, however, disclose that this biological material is freely available to the public, either currently or upon the issuance of a patent having the biological materials as subject matter embraced by claim 49. Deposits under the terms of the Budapest Treaty are, in themselves, insufficient to satisfy 37 CFR §§ 1.805-1.807 unless they are disclosed on the record to be freely available to the public should a U.S. patent issue on the instant application. See, *Ex parte Hildebrand*, 15 USPQ2d 1662, 1664 (1990) (restrictions must "be irrevocably removed upon the issuance of [a] patent" since Rule 9.2 of the Budapest Treaty contains a residual requirement of secrecy). See also, MPEP § 608.01(p)(C)(3). Application of 37 CFR § 1.801, et seq., to any deposit, including Budapest Treaty deposits, requires that an enabling disclosure based upon such a deposit be provided by submission of a declaration or averment, either by the **assignee** or the **attorney of record** over his or her signature and registration number, that gives these two assurances:

1) that all restrictions on the availability to the public of the deposited material will be removed, and,
2) that the viability of the deposits will be maintained,

both for the duration of the patent term or for a period of twenty years in accordance with 37 CFR §§ 1.805-1.807. See, MPEP §§ 2405-2411.05, wherein the latter section requires an amendment to the specification that introduces specific information concerning any deposit of biological materials. Such an amendment does not constitute new matter.

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 8-11, 14, 19-22, and 49 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected as indefinite because there are many conditions that may be considered to constitute "low stringency" hybridization conditions, e.g., those set forth at page 14, lines 20-34, of the specification, but none are required by the claim. Thus the public and the artisan cannot determine the meets and bounds of claim 1, and of claims 1, 14, 19-22, and 49 that depend therefrom but do not otherwise state any particular "low stringency" hybridization conditions, thus are included in this rejection. While claim 8 does not depend from claim 1, it too is rejected because, absent a structural limitation defining the extent of structural alteration of SEQ ID NO:2, the public and the artisan cannot determine the meets and bounds of alterations of the claim.

Claims 8-11 are rejected as indefinite because claim 8, from which claims 9-11 depend recites "of one or more amino acid residues", a phrase that removes any metes and bounds from the claimed subject matter by permitting replacement of the entire amino acid sequence of SEQ ID NO:2. Thus, for purposes of examination, these claims are assumed to be directed to any subtilase. Claims 19-11 are included in this rejection because they depend claim 9 but fail to resolve its ambiguity with respect to positions beyond those recited in the claims. This aspect of the rejection may be overcome by deleting claim 8 and making claim 9 the independent claim – as modified according to the following paragraph – beginning with a recitation such as "[a] subtilase comprising a mutation which is a substitution, deletion, or insertion of an amino acid in the amino acid sequence of SEQ ID NO:2 at one or more of the amino acid positions . . . wherein each position corresponds to a position in ~~of~~ the amino acid sequence of the mature subtilisin BPN' set forth in SEQ ID NO:9.

Claims 9-11 are rejected as indefinite where claim 9, from which claims 10 and 11 depend, recites no sequence identifier for the amino acid sequence to which it refers,

that of the mature subtilisin BPN', thus fails to particularly point out and distinctly claim Applicant's intended subject matter by failing to place recited positions for substitution, insertion, or deletion in the context of a particular amino acid sequence. Claims 10 and 11 are subject to this rejection because they depend claim 9 but fail to resolve its ambiguity. This aspect of the rejection may be overcome by amending claim 9 to insert a clause that states the absent sequence identifier, e.g., "wherein each position corresponds to a position in ~~of~~ the amino acid sequence of the mature subtilisin BPN' set forth in SEQ ID NO:9.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. § 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. § 122(b). Therefore, this application is examined under 35 U.S.C. § 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. § 102(e)).

Although the scope of claim 1 as construed at pages 4-5 hereinabove embraces the amino acid sequences of a great number of prior art subtilases, including the amino acid sequence of the mature subtilisin BPN' set forth in SEQ ID NO:9 herein which shares 57.3% sequence identity with SEQ ID NO:2 recited in claim 1 herein, only publications that disclose modified subtilases meeting limitations of at least claims 1, 8-10, 14, 19, 21, and 49 are cited herein to avoid undue, duplicative, citations of the prior art.

Claims 1, 8-10, 14, 19, 21, and 49 are rejected under 35 U.S.C. § 102(b) as being anticipated by Christianson et al., US Patent No. 5,500,364, made of record with Applicant's Information Disclosure Statement.

Christianson et al. disclose multiple modifications of the amino acid sequence of a *Bacillus lentus* subtilase which, prior to modification, shared over 87% identity with the amino acid sequence set forth in SEQ ID NO:2 herein, to introduce, see Table 2, amino acid substitutions at positions 96, 101, 102, 118, 130, 141, 157, 188, 229, 242, and 268, which correspond to positions 98, 103, 104, 120, 132, 143, 159, 194, 235, 248 and 274 of the amino acid sequence of subtilisin BPN' set forth in SEQ ID NO:9 herein, meeting limitations of claims 1, 8, 9, and 14 where anticipation of claim 14 is inherent because the modified subtilases of Christianson et al., meet the structural limitations of claim 1. Christianson et al. also anticipate claim 10 in disclosing, Table 2, the substitution A194 because their A188P substitution occurs at the subtilisin BPN'-correspondent position 194. Christianson et al. further anticipate claims 19 and 21 in disclosing, cols. 1 and 2, the incorporation of any subtilase in "detergent formulations", and the use of such compositions in washing laundry. Christianson et al. additionally anticipate the subject matter of claim 49 in disclosing, in Examples 4-8, the culture of *Bacillus* strains expressing the native and modified subtilases and the recovery and purification of the secreted subtilases from the culture supernatant.

Claims 1, 8-11, 14, 19-21, and 49 are rejected under 35 U.S.C. § 102(b) as being anticipated by Hansen et al., WO 99/27082, made of record with Applicant's Information Disclosure Statement.

Hansen et al. disclose multiple modifications of the amino acid sequence of a *Bacillus lentus* subtilase which, prior to modification, shared over 87% identity with the amino acid sequence set forth in SEQ ID NO:2 herein, to introduce, see page 23 and claims 16-18 and 21, amino acid insertions and substitutions, and sets thereof, at many of the subtilisin BP'-correspondent positions recited in claims 9-11 herein including K27R, *36D, V104N, V104I, N123S, Y167A, R170S, Q206E, N218S, M222S, M222A,

T224S, K235L, and T274A, and substitutions at position 87, 97, 101, 120, and 218, as well as the first three sets of claim 11 herein, meeting limitations of claims 1, 8-11, and 14 where anticipation of claim 14 is inherent because the modified subtilases of Hansen et al., meet the structural limitations of claim 1. Hansen et al. further anticipate claims 19-21 in disclosing, pages 29-60 and claims 28-31, the incorporation of their modified subtilases in cleaning and detergent compositions that additionally comprise one or more of an amylase, cellulase, cutinase, lipase, oxidoreductase, and other proteases for use in methods of cleaning of washing laundry. Hansen et al. additionally anticipate the subject matter of claim 49 in disclosing, in Examples 1 and 2, the culture of *Bacillus* strains expressing the modified subtilases and the subsequent recovery and purification of the secreted subtilases from the culture supernatant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 22 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Hansen et al., as applied to claims 1, 8-11, 14, and 19-21 above, in view of Maurer et al., US Patent No. 5,855,625, made of record herewith.

The teachings of Hansen et al., discussed above, are taken as before. Maurer et al. teach cols. 2-8, that while detergent compositions comprising native *Bacillus lentus* subtilases are quite effective in removing egg stains from fabrics, that compositions comprising native *Bacillus lentus* subtilases having an amino acid substitution at the subtilisin BPN'-correspondent position 217 – position 211 in a *Bacillus lentus* subtilase – are "particularly effective" in removing egg stains from fabrics. Maurer et al. teach that additional amino acid substitutions at the subtilisin BPN-correspondent position 101 –

position 99 in a *Bacillus lentus* subtilase – including the subtilisin BPN-correspondent R101G substitution recited in claim 9 herein make a *Bacillus lentus* subtilase even more effective in removing egg stains from fabrics, see claims 20 and 23. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the modified subtilases of Hansen et al. in the methods of claims 20 and 23 of Maurer et al., corresponding to the method of claim 22 herein, because Hansen et al. teach modified subtilases comprising the modifications made by Maurer et al. as well as additional modifications that make them useful in detergent compositions applied in methods of removing stains from fabrics generally.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is now 571.272.0933. The examiner can normally be reached between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can now be reached at 571.272.0928. The fax phone numbers for all communications for the organization where this application or proceeding is assigned remains 703.872.9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is now 571.272.1600.

William W. Moore
November 29, 2004

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600